REMARKS

I. Status Summary

Claims 1-19 are pending in the present application. Election by applicants of Group I, claims 1-17 has been acknowledged by the U.S. Patent and Trademark Office (hereinafter "the Patent Office") and claims 1-17 presently examined. Claims 18-19 have been withdrawn from prosecution at this time. Claims 1, 9, and 16 have been amended. Claims 4 and 11 have been canceled.

The specification has been objected to for allegedly failing to provide proper antecedent basis for the claimed subject matter. The specification has also been objected to for allegedly failing to comply with 37 CFR §§ 1.821-1.825 for not including sequence identifiers for nucleic acid sequences and amino acid sequences set forth in Figure 1 and for not including these sequences in the Sequence Listing.

Claims 1, 2, 4, 9, and 11 presently stand rejected under 35 USC § 102(b) as allegedly being anticipated by U.S. Patent No. 5,252,466 to Cronan (hereinafter "Cronan"). Claims 1, 2, 4-9, and 11-16 presently stand rejected under 35 USC § 103(a) as allegedly being obvious over Cronan in view of the journal article to Rigaut *et al.* (Nature Biotech., 17: 1030-1032, 1999; hereinafter "Rigaut *et al.*"). Claims 1-16 presently stand rejected under 35 USC § 103(a) as allegedly being obvious over Cronan in view of Rigaut *et al.* and further in view of U.S. Patent No. 6,114,111 to Luo *et al.* (hereinafter "Luo *et al.*"). Claims 1-17 presently stand rejected under 35 USC § 103(a) as allegedly being obvious over Cronan in view of Rigaut *et al.*, further in view of Luo *et al.*, and further in view of U.S. Patent No. 5,283,173 to Fields *et al.* (hereinafter "Fields *et al.*").

II. Response to Objection to Specification

The Patent Office has objected to the specification as failing to provide proper antecedent basis for the claimed subject matter, contending that claim 16 recites "a plurality of potential binding partners" and claim 17 recites "a plurality of potential

binding partners" and "a plurality of nucleic acid expression vectors", none of which allegedly are supported by the specification as filed.

The specification has been amended as indicated by the amendment above to provide support for the terms. Support for the amendment to the specification can be found in original claims 16 and 17. As such, no new matter has been added by the amendment.

The Patent Office has also objected to the specification as containing nucleotide and amino acid sequences that do not include sequence identifiers. In particular, the Patent Office contends Figure 1 includes a polynucleotide sequence and a polypeptide sequence; however, the specification does not provide sequence identifiers for these sequences.

The specification has been amended as indicated in the amendment above to include sequence identifiers for both these sequences, now referenced as SEQ ID NO: 7 and SEQ ID NO:8. Additionally, a revised Sequence Listing is attached hereto that includes SEQ ID NOs: 7 and 8. Support for the amendment can be found in Figure 1 as filed, which discloses the sequences. As such, no new matter has been added by the amendment.

In view of the above amendments and remarks, applicants respectfully request withdrawal of the objections to the specification.

III. Response to the Rejections Under 35 U.S.C. § 102

Claims 1, 2, 4, 9, and 11 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Cronan. The Patent Office contends Cronan teaches a method for obtaining *in vivo* binding partners of a protein comprising obtaining a transformed host cell and expressing a fusion protein comprising a protein of interest and a post-translation biotination sequence; growing the cell under conditions to permit expression and modification; contacting the cell extract with an affinity purification reagent; and separating the complex from the extract. The Patent Office further contends Cronan teaches the fusion protein is a heterologous protein, and

there is a cleavage site between the protein of interest and the post-translation biotination sequence. The Patent Office still further contends Cronan teaches identifying more than one binding partner, as well as transforming a cell with a vector encoding the fusion protein. The Patent Office therefore contends Cronan teaches every step of each of rejected claims 1, 2, 4, 9, and 11.

The position of the Patent Office as summarized above with respect to claims 1, 2, 4, 9, and 11 is respectfully traversed as described below.

"A claim is anticipated only if each and every element in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Independent claim 1 presently recites a method for obtaining *in vivo* binding partners of a protein of interest in a cell type, comprising: obtaining a cell of said cell type transformed to express a fusion protein, said fusion protein comprising: said protein of interest; and a post-translational modification sequence; growing said cell or progeny of said cell under conditions which permit expression and post-translation modification of said fusion protein to produce a tagged fusion protein; contacting an extract of said cell or progeny of said cell with an affinity purification reagent which specifically binds to said tagged fusion protein to form a complex; separating said complex from said extract; and identifying any binding partners that bind said protein of interest in said complex.

Claim 1 has been amended to more particularly recite in part that binding partners are identified that can bind the protein of interest and thereby co-separate with the tagged fusion protein and the affinity purification reagent in the complex. Support for the amendment can be found throughout the specification, including, for example in claim 4 as originally filed and at page 4, lines 17-19 of the specification as filed.

Independent claim 9 presently recites a method for obtaining *in vivo* binding partners of a protein of interest in a cell type, comprising: transforming a cell of said

cell type with a vector encoding a fusion protein, the fusion protein comprising: said protein of interest; a post-translational modification sequence; growing said cell or progeny of said cell under conditions which permit expression and post-translation modification of said fusion protein to produce a tagged fusion protein; contacting an extract of said cell or progeny of said cell with an affinity purification reagent which specifically binds to said tagged fusion protein to form a complex; separating said complex from said extract; and identifying any binding partners that bind said protein of interest in said complex.

Claim 9 has been amended to more particularly recite in part that binding partners are identified that can bind the protein of interest and thereby co-separate with the tagged fusion protein and the affinity purification reagent in the complex. Support for the amendment can be found throughout the specification, including, for example in claim 11 as originally filed and at page 4, lines 28-30 of the specification as filed.

The Patent Office contends that Cronan teaches a method for obtaining *in vivo* binding partners of a protein comprising expressing a fusion protein comprising a protein of interest and a post-translation biotination sequence; growing the cell under conditions that permit expression and modification; contacting the cell extract with an affinity purification reagent; and separating the complex from the extract to obtain *in vivo* binding partners of the protein (see pages 3 and 4 of the Official Action). Applicants respectfully disagree with the Patent Office's interpretation of the teachings of Cronan.

Cronan at best teaches isolating the modified fusion protein by providing a binding partner that binds to the fusion protein only after the fusion protein has been post-translationally modified. See Cronan Abstract; Field of Invention; and col. 5, l. 65 – col. 6, l. 29. The term "binding partner" referred to in Cronan does not refer to binding partners of the protein of interest, but rather to molecules that bind to the post-translational modification. For example, Cronan teaches that when the fusion protein is post-translationally modified with biotin, the "binding partner" can be avidin,

streptavidin, or an antibody to biotin. See Cronan at col. 6, l. 10-16 and col. 13, l. 55 – col. 14, l. 27. Thus, Cronan only teaches isolating the fusion protein itself and does not therefore appear to teach identifying any binding partners that bind the protein of interest within the fusion protein, as recited in the present pending claims. As such, Cronan does not teach each and every element of claims 1 and 9.

Since Cronan does not teach each and every element of claims 1 and 9, applicants respectfully request withdrawal of the rejection of claim 1 under 35 U.S.C. § 102(b) as being anticipated by Cronan. Allowance of claims 1 and 9 is also respectfully requested.

With regard to the rejection of claims 2, 4, and 11, applicants initially note claims 4 and 11 have been canceled, thereby rendering the rejection of these claims moot. With regard to the rejection of claim 2, applicants contend that Cronan does not teach all the elements of this claim. Since claim 2 depends from claim 1, and Cronan does not teach or suggest all the elements of claim 1 for the reasons stated above, Cronan therefore does not teach or suggest all the elements of claim 2 either. Accordingly, applicants respectfully request withdrawal of the rejection of claim 2 on the basis of Cronan. Allowance of claim 2 is also respectfully requested.

IV. Response to the Rejections Under 35 U.S.C. § 103

IV.A. Cronan in view of Rigaut et al.

Claims 1, 2, 4-9, and 11-16 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Cronan in view of Rigaut *et al.*

The Patent Office alleges that Cronan teaches each and every element of the rejected claims, except the Patent Office concedes that the cited reference does not specifically teach affinity tagging the fusion protein, or cleaving the protein of interest from the post-translational modification sequence prior to identifying binding partners of the protein of interest. However, the Patent Office alleges that Rigaut *et al.* teaches a transformed yeast cell with a fusion protein comprising a heterologous protein with two affinity tags, a *S. aureus* protein A IgG binding domain and a

calmodulin binding peptide, as well as a TEV cleavage site. The Patent Office further contends Rigaut *et al.* teaches the target protein can be cleaved from the post-translational modification sequence prior to identifying binding partners of the target protein. The Patent Office argues it would have been obvious to one of skill in the art at the time the claimed invention was made to combine the teachings of the two references.

After careful consideration of the rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection and submit the following remarks.

Initially, applicants submit that to establish *prima facie* obviousness, each and every claim limitation must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Applicants respectfully submit that independent claims 1, 9, and 16 have been amended herein to recite, in part, methods for identifying binding partners of a protein of interest by expression in a cell of a fusion protein comprising the protein of interest and a post-translational modification sequence, and post-translation modification of the fusion protein to produce a tagged fusion protein; contacting an extract of the cell or progeny of the cell with an affinity purification reagent which specifically binds to the tagged fusion protein to form a complex; and identifying binding partners of the protein of interest that bind the protein of interest in the complex. Further, claim 16 recites introducing into the cell the plurality of potential binding partners.

Support for the amendment to claims 1, 9, and 16 can be found throughout the specification as filed, including particularly in claims 4 and 11 as filed and at page 18, lines 15-26 of the present specification. No new matter has been added.

As previously discussed hereinabove, Cronan only teaches isolating the fusion protein itself. Applicants respectfully submit Cronan does not teach identifying any binding partners that bind the protein of interest within the fusion protein, as recited in the present pending claims. Further, with regard to claim 16, Cronan also does not appear to teach introducing into the cell the plurality of potential binding partners.

Rigaut *et al.* does not support the deficiencies of Cronan. Rigaut *et al.* appears to at best teach a method of protein purification by expressing a fusion protein comprising a target protein to be purified fused to a tag peptide, wherein the tag peptide is targeted for purification of the target protein. Rigaut *et al.* does not appear to teach utilizing a fusion protein comprising a protein of interest and a post-translational modification sequence, which after expression and post-translation modification, can identify any binding partners that bind the protein of interest in a co-purified complex. Rigaut *et al.* also does not appear to teach introducing into the cell the plurality of potential binding partners.

Further, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Prior art references must be considered in their entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984). Since Cronan does not teach or suggest identifying any binding partners that bind the protein of interest within the fusion protein, one of ordinary skill in the art desiring to identify binding partners of a protein of interest utilizing a fusion protein comprising an affinity purification sequence would not be motivated to turn to Cronan to look for desired components, since Cronan does not teach or suggest a key component of the endeavor, that is, identifying binding partners of a protein of interest. As such, applicants respectfully submit there is no suggestion or motivation to combine the teachings of Cronan and Rigaut *et al.*

Thus, applicants respectfully submit that neither Cronan nor Rigaut *et al.* alone teach or suggest each and every element of pending independent claims 1, 9, and 16. Further, applicants respectfully submit there is no motivation to combine the teachings of Cronan and Rigaut *et al.* Accordingly, applicants submit that the cited combination does not support the instant rejection of claims 1, 9, and 16. Hence,

applicants respectfully submit that a *prima facie* case of obviousness has not been established, and applicants respectfully request the instant rejection of claims 1, 9, and 16 under 35 U.S.C. § 103(a) be withdrawn. Allowance of these claims is also respectfully requested.

With regard to the rejection of claims 2, 4-8, and 11-15, applicants initially note claims 4 and 11 have been canceled, thereby rendering the rejection of these claims moot. With regard to the rejection of claims 2, 5-8, and 12-15 applicants contend that Cronan and Rigaut *et al.*, either alone or in combination, do not teach or suggest all the elements of these claims. Since claims 2, 5-8, and 12-15 depend directly or indirectly from claims 1, 9, or 16, and Cronan and Rigaut *et al.*, either alone or in combination do not teach or suggest all the elements of claims 1, 9, or 16 for the reasons stated above, Cronan and Rigaut *et al.* therefore do not teach or suggest all the elements of these dependent claims either. Accordingly, applicants respectfully request withdrawal of the rejection of claims 2, 5-8, and 12-15 on the basis of Cronan in view of Rigaut *et al.* Allowance of these claims is also respectfully requested.

IV.B. Cronan in view of Rigaut et al. and in further view of Luo et al.

Claims 1-16 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Cronan in view of Rigaut *et al.* and further in view of Luo *et al.*

The Patent Office alleges that Cronan and Rigaut *et al.* together teach or suggest each and every element of the rejected claims as disclosed hereinabove, except the Patent Office concedes that the cited references do not specifically teach the use of a mammalian cell containing a fusion protein. However, the Patent Office alleges that Luo *et al.* does teach the use of a mammalian cell containing a fusion protein. The Patent Office argues it would have been obvious to one of skill in the art at the time the claimed invention was made to combine the teachings of the three references.

After careful consideration of the rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection and submit the following remarks.

As previously noted, independent claims 1, 9, and 16 have been amended herein to recite, in part, methods for identifying binding partners of a protein of interest by expression in a cell of a fusion protein comprising the protein of interest and a post-translational modification sequence, and post-translation modification of the fusion protein to produce a tagged fusion protein; contacting an extract of the cell or progeny of the cell with an affinity purification reagent which specifically binds to the tagged fusion protein to form a complex; and identifying binding partners of the protein of interest that bind the protein of interest in the complex. Also as previously noted, claim 16 further recites introducing into the cell the plurality of potential binding partners.

As previously discussed hereinabove, Cronan and Rigaut *et al.* do not teach or suggest every element of any of the rejected claims. Specifically, Cronan does not teach identifying any binding partners that bind the protein of interest within the fusion protein, as recited in the present pending claims. Further, Rigaut *et al.* does not teach or suggest a fusion protein comprising a protein of interest and a post-translational modification sequence, which after expression and post-translation modification, can be utilized to identify any binding partners that bind the protein of interest in a co-purified complex. Additionally, with regard to claim 16, neither Cronan nor Rigaut *et al.* appear to teach introducing into the cell the plurality of potential binding partners. Finally, as previously discussed hereinabove, there does not appear to be a valid suggestion or motivation to combine the teachings of Cronan and Rigaut *et al.*

Applicants respectfully submit Luo *et al.* does not cure these deficiencies. Specifically, Luo *et al.* does not recite a method of utilizing a fusion protein comprising a protein of interest and a post-translational modification sequence, which after expression and post-translation modification, can identify any binding partners

that bind the protein of interest in a co-purified complex. Rather, Luo *et al.* appears to at best teach utilizing two fusion proteins, the first of which contains a DNA binding domain fused to a "bait" protein and the second of which consists of a transcriptional activation domain fused to a "test" protein, to analyze protein-protein interactions between known proteins and to isolate and characterize unknown protein.

Thus, applicants respectfully submit that Cronan, Rigaut *et al.*, and Luo *et al.* do not teach or suggest, alone or in combination, each and every element of pending independent claims 1, 9, and 16. Accordingly, applicants submit that the cited combination does not support the instant rejection of claims 1, 9, and 16. Hence, applicants respectfully submit that a *prima facie* case of obviousness has not been established, and applicants respectfully request the instant rejection of claims 1, 9, and 16 under 35 U.S.C. § 103(a) be withdrawn. Allowance of these claims is also respectfully requested.

With regard to the rejection of claims 2-8, and 10-15, applicants again note claims 4 and 11 have been canceled, thereby rendering the rejection of these claims moot. With regard to the rejection of claims 2, 3, 5-8, 10, and 12-15 applicants contend that Cronan, Rigaut *et al.*, and Luo *et al.*, either alone or in combination, do not teach or suggest all the elements of these claims. Since claims 2, 3, 5-8, 10, and 12-15 depend directly or indirectly from claims 1, 9, or 16, and Cronan, Rigaut *et al.*, and Luo *et al.*, either alone or in combination do not teach or suggest all the elements of claims 1, 9, or 16 for the reasons stated above, Cronan, Rigaut *et al.*, and Luo *et al.* therefore do not teach or suggest all the elements of these dependent claims either. Accordingly, applicants respectfully request withdrawal of the rejection of claims 2, 3, 5-8, 10, and 12-15 on the basis of Cronan in view of Rigaut *et al.* and further in view of Luo *et al.* Allowance of these claims is also respectfully requested.

IV.C. Cronan in view of Rigaut et al., in view of Luo et al. and in further view of Fields et al.

Claims 1-17 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Cronan in view of Rigaut *et al.*, in view of Luo *et al.*, and further in view of Fields *et al.*

The Patent Office alleges that Cronan, Rigaut *et al.*, and Luo *et al.* together teach or suggest each and every element of the rejected claims as disclosed hereinabove, except the Patent Office concedes that the cited references do not specifically teach the use of a plurality of potential binding partners encoded by a plurality of nucleic acid expression vectors. However, the Patent Office alleges that Fields *et al.* does teach this element in that Fields *et al.* teaches a library of cDNA plasmids for a yeast two-hybrid assay. The Patent Office argues it would have been obvious to one of skill in the art at the time the claimed invention was made to combine the teachings of the four references.

After careful consideration of the rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection and submit the following remarks.

As previously discussed, independent claims 1, 9, and 16 have been amended herein to recite, in part, methods for identifying binding partners of a protein of interest by expression in a cell of a fusion protein comprising the protein of interest and a post-translational modification sequence, and post-translation modification of the fusion protein to produce a tagged fusion protein; contacting an extract of the cell or progeny of the cell with an affinity purification reagent which specifically binds to the tagged fusion protein to form a complex; and identifying binding partners of the protein of interest that bind the protein of interest in the complex.

As previously discussed hereinabove, Cronan, Rigaut *et al.*, and Luo *et al.* do not each teach or suggest every element of any of the rejected claims. Specifically, Cronan does not teach identifying any binding partners that bind the protein of interest within the fusion protein, as recited in the present pending claims. Further,

Rigaut *et al.* and Luo *et al.* do not teach or suggest a method of utilizing a fusion protein comprising a protein of interest and a post-translational modification sequence, which after expression and post-translation modification, can identify any binding partners that bind the protein of interest in a co-purified complex. Still further, with regard to claim 16, Cronan, Rigaut *et al.*, and Luo *et al.* do not appear to teach or suggest introducing into the cell the plurality of potential binding partners. Finally, as previously discussed hereinabove, there does not appear to be a valid suggestion or motivation to combine the teachings of Cronan and Rigaut *et al.*

Applicants respectfully submit Fields *et al.* does not cure these deficiencies. Fields *et al.* also does not recite a method of utilizing a fusion protein comprising a protein of interest and a post-translational modification sequence, which after expression and post-translation modification, can identify any binding partners that bind the protein of interest in a co-purified complex. Rather, Fields *et al.* at best appears to teach a yeast two-hybrid system to detect pair-wise protein-protein interactions via transcriptional activation of a reporter gene.

Thus, applicants respectfully submit that Cronan, Rigaut *et al.*, Luo *et al.*, and Fields *et al.* do not teach or suggest, alone or in combination, each and every element of pending independent claims 1, 9, and 16. Accordingly, applicants submit that the cited combination does not support the instant rejection of claims 1, 9, and 16. Hence, applicants respectfully submit that a *prima facie* case of obviousness has not been established, and applicants respectfully request the instant rejection of claims 1, 9, and 16 under 35 U.S.C. § 103(a) be withdrawn. Allowance of these claims is also respectfully requested.

With regard to the rejection of claims 2-8, 10-15, and 17, applicants again note claims 4 and 11 have been canceled, thereby rendering the rejection of these claims moot. With regard to the rejection of claims 2, 3, 5-8, 10, 12-15, and 17, applicants contend that Cronan, Rigaut *et al.*, Luo *et al.*, and Fields *et al.*, either alone or in combination, do not teach or suggest all the elements of these claims. Since claims 2, 3, 5-8, 10, 12-15, and 17 depend directly or indirectly from claims 1, 9, or 16, and

Cronan, Rigaut *et al.*, Luo *et al.*, and Fields *et al.*, either alone or in combination do not teach or suggest all the elements of claims 1, 9, or 16 for the reasons stated above, Cronan, Rigaut *et al.*, Luo *et al.*, and Fields *et al.* therefore do not teach or suggest all the elements of these dependent claims either. Accordingly, applicants respectfully request withdrawal of the rejection of claims 2, 3, 5-8, 10, 12-15, and 17 on the basis of Cronan in view of Rigaut *et al.* and Luo et al and further in view of Fields *et al.* Allowance of these claims is also respectfully requested.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

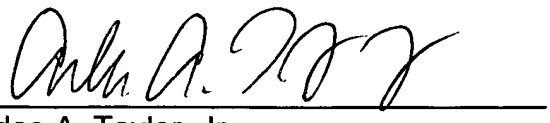
If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any fees associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,

JENKINS, WILSON, TAYLOR & HUNT, P.A.

Date: June 30, 2006 By: 

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